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CASE REPORT

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Tubulointerstitial lesions converted into lupus nephritis

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Abstract

A young woman was diagnosed with SLE and Sjögren's syndrome with tubulointerstitial lesions and remained stable after prednisone treatment. However, repeat renal biopsy after prednisone withdrawal revealed it was converted into glomerular lesions.

KEYWORDS

renal biopsy, systemic lupus erythematosus, tubulointerstitial lesion

1 | INTRODUCTION

The presence of glomerular injuries is the main pathogenetic factor of renal impairment in systemic lupus erythematosus (SLE), while predominant tubulointerstitial lesions are rare in SLE.[1,2] Although some cases of predominant tubulointerstitial lesion have been reported in patients with SLE,[3] there were few cases with follow-up outcome of long-term treatment, especially for patients with repeat renal biopsy results.[4] We present a case of SLE with Sjögren's syndrome and onset predominant tubulointerstitial lesions, who was followed up for more than eight years. The patient recovered soon after the treatment of prednisone and had a good condition in the following 6 years. Then, the patient stopped the treatment of prednisone for one year. The repeat renal biopsy results revealed progressive changes from onset tubulointerstitial lesions to glomerulonephritis, although it is common that SLE glomerular lesions may be converted from one class to another.[5] To the best of our knowledge, such case with a follow-up repeat renal biopsy result after more than eight years has never been reported in literature to date.

2 | CASE REPORT

A 36-year-old woman was admitted to our hospital with arthralgia, oral ulcers, fatigue, and polyuria for two months eight years ago. Physical examination was unremarkable except for the oral ulcers. Biochemical and immunological test results showed the following: serum glucose, 4.8 mmol/L; urine specific gravity, 1.003, with no proteinuria or hematuria; 24-hour urine protein, 0.12 g; serum creatinine, 1.8 mg/dL; hemoglobin (Hb), 81 g/L, white blood cell (WBC) count, 3.84×10^9/L, platelet, 96×10^9/L; erythrocyte sedimentation rate (ESR), 90 mm/h; positivity for antinuclear antibodies (ANA, 1:10 000), anti-dsDNA (316.83 IU/mL, the normal range is <100 IU/mL), and Sm antibody; component 3 (C3), 70 mg/L (normal range: 790-1520 mg/L) and

component 4 (C4), 86 mg/L (normal range: 100-400 mg/L); and negative anti-SS antigen A (SS-A) and anti-SS antigen B (SS-B). Water deprivation test revealed a 24-hour urinary volume of 4.5 L, and there was a minimal increase in urine osmolality from 124 to 146 mOsm/kg after giving vasopressin, indicating nephrogenic diabetes insipidus. The percutaneous renal biopsy disclosed 11 normal glomeruli and no glomerular basement membrane injury, and two glomeruli with minimal mesangial proliferation. The interstitium was mildly edema with dense plasmacyte infiltrates, interstitial fibrosis, and severe tubular atrophy (Figures 1 and 2). The immunofluorescence microscopy revealed the negative staining of immunoglobulins and complements in the renal tissue. At six months before admission to our hospital, the patient was diagnosed with Sjögren's syndrome in another hospital due to the complaint of dry eyes and xerostomia**,** and th**e** lip biopsy results revealed focal lymphocytic infiltration of the minor salivary glands (Figure 3). The patient refused treatment at that time. According to the abovementioned description, the patient was diagnosed with SLE and Sjögren's syndrome based on the European League Against Rheumatism and the American College of Rheumatology (EULAR/ACR) criteria, and the disease activity score is 12 according to systemic lupus erythematosus disease activity index (SLEDAI) score. Prednisone (30 mg/d) was administered, and the patient recovered after four weeks with normal serum creatinine, urine specific gravity, Hb, WBC count, platelet, C3 and C4, and without dry eyes and xerostomia. The patient was followed up regularly. The prednisone dose was gradually tapered and maintained at the dose of 5 mg/d. Finally, the patient's condition remained stable.

However, the patient discontinued the prednisone treatment by herself and refused to take it again after six years. After one year, the patient developed arthralgia, hair loss, fatigue, and oral ulcers, and the laboratory test results revealed the following: 24-hour urine protein, 1.4 g; serum creatinine, 1.2 mg/dL; ESR, 105 mm/h; positivity for ANA (1:3,200), anti-dsDNA (427 IU/mL, normal range: <100 IU/mL), and Sm antibody; C3, 56 mg/L (normal range: 790-1520 mg/L) and C4, 82 mg/L (normal range:18-400 mg/L); and negative SS-A and SS-B. The disease activity score is 16 (SLEDAI score). Repeat renal biopsy results showed 19 glomeruli, three entirely sclerotic, and one cellular crescent. There was moderate segmental mesangial proliferation with a thickening glomerular basement membrane and spike formation (Figure 2). However, there was a minimal tubulointerstitial lesion (Figure 1C,D). The immunofluorescence microscopy revealed dense staining with fine granular distribution for IgG, IgM, IgA, and C3 in the mesangium region. Prednisone (30 mg/d) was re-administered, and the patient gradually recovered. The patient had normal serum creatinine, ESR, C3, and C4 without proteinuria after two months. Her most recent follow-up showed her to be well.

3 | DISCUSSION

In patients with lupus nephritis, glomerular lesions are the main renal involvement. Therefore, the World Health Organization (WHO) classification of lupus nephritis was based exclusively on glomerular lesions.[6] Tubulointerstitial involvement has been

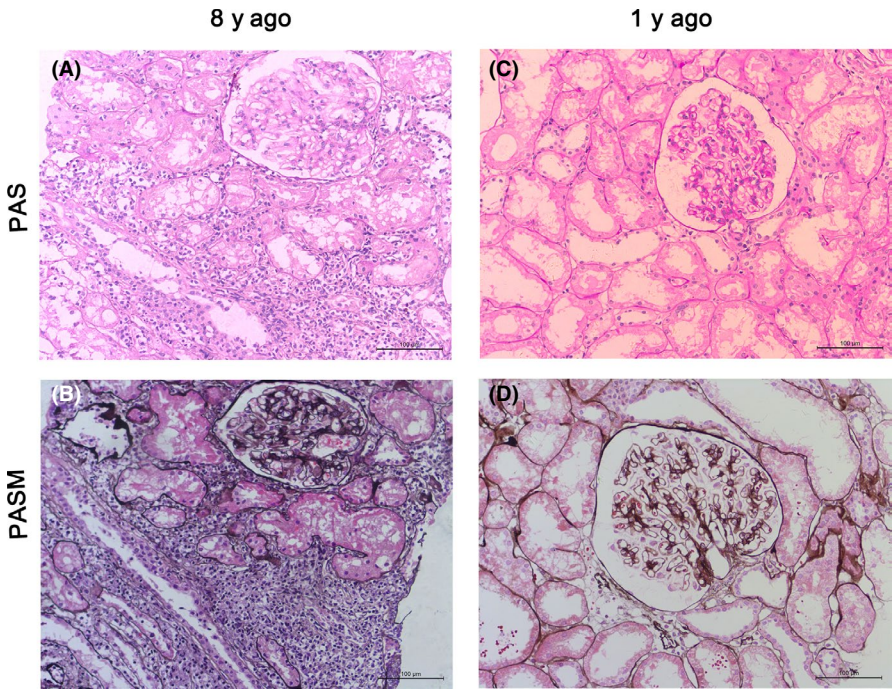

FIGURE 1 Renal histopathology of Periodic acid-Schiff staining (PAS) and periodic Schiff-methenamine staining (PASM) showed severe interstitial fibrosis, tubular atrophy, and minimal mesangial cell proliferation eight years ago (A and B), moderate mesangial cell proliferation with minimal tubulointerstitial injuries one year ago (C and D). (Bar = 100 μm)

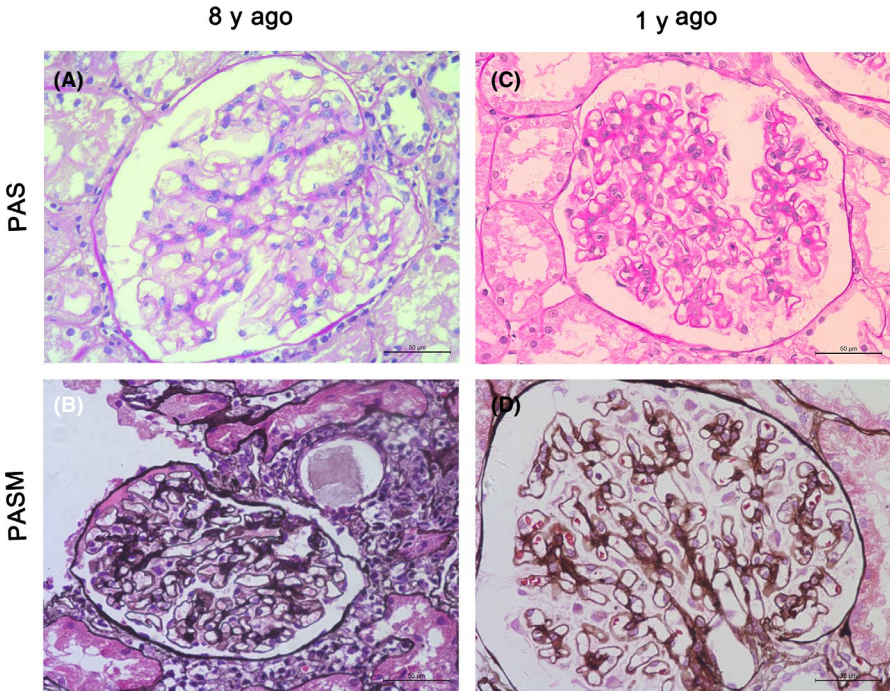

FIGURE 2 Periodic acid-Schiff staining (PAS) showed minimal mesangial proliferative lesions eight years ago (A) and moderate mesangial proliferative lesions one year ago (C). Periodic Schiff-methenamine staining (PASM) showed no glomerular basement membrane injury eight years ago (B) and thickening glomerular basement membrane with subepithelial spike formation (D). (Bar = 50 μm)

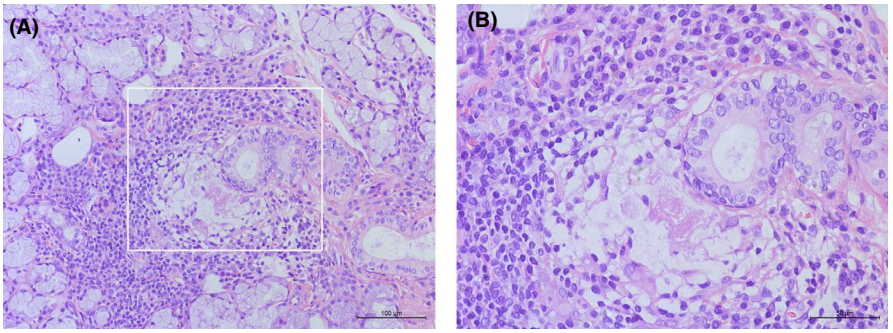

FIGURE 3 Lip biopsy results showing focal lymphocytic infiltration of the minor salivary glands. (A, bar = 100 μm; B, bar = 50 μm)

observed in approximately two-thirds of lupus nephritis patients,[3,7] and this is often accompanied by severe glomerular lesions, although it is not included in the classification system. However, it has been reported that there were only 13 cases of predominant tubulointerstitial lupus nephritis in literatures written in the English language, indicating that predominant tubulointerstitial nephritis is rare.[1,8] The present case did not provide any evidence of glomerular lesion from the onset urine analysis, suggesting a tubulointerstitial lesion. The percutaneous renal biopsy results revealed interstitial fibrosis and heavy atrophy of the renal tubules with minimal glomerular impairment. It was reported that almost one-fifth of SLE patients have concomitant Sjögren's syndrome; however, the present patient suffered from Sjögren's syndrome six months early before SLE was established, and Sjögren's syndrome may be secondary to SLE according to the progression of the disease in the present case. In addition, the patient never received other medication treatment, such as nonsteroidal anti-inflammatory drugs. Furthermore, there were no drug-induced interstitial injuries in the present case. Although predominant tubulointerstitial nephritis was established in the present case, it is different from other reported cases. There was deposition of immunoglobulins or complements along the tubular basement membranes in the previous cases of predominant tubulointerstitial nephritis. However, the immunofluorescence results in the present case showed the negative staining of immunoglobulins and complements in the renal tissue. The reason may be that the tubulointerstitial lesion in the present case was caused by Sjögren's syndrome diagnosed at six months early before SLE was established, although this is rare in patients with SLE and Sjögren's syndrome.[1]

In the present case, another main characteristic is that the onset renal pathological lesion was converted into different pathological changes after seven years. It is well-known that glomerular lesions in patients with lupus nephritis may be converted from one class to another.[5] However, for the present case, the onset of tubulointerstitial lesions was changed to predominant glomerulonephritis, suggesting progressive pathological changes due to prednisone withdrawal for one year. The repeat renal biopsy revealed the conversion from tubulointerstitial nephritis to glomerulopathy in the present case with SLE and Sjögren's syndrome, which is a special type of pathological change. The reason may be Sjögren's syndrome

secondary to SLE, which impaired the kidneys, mainly showing tubulointerstitial lesions without changes in glomerulus. As we all know, there may be few changes in the very early stage of typical lupus nephritis, so there was also few glomerular lesion in the initial pathological changes in the present case. However, SLE was diagnosed shortly after Sjögren's syndrome, and Sjögren's syndrome was thought to be secondary to SLE in the present case, then tubulointerstitial lesions caused by Sjögren's syndrome occurred in the early stage of the patient. To our best knowledge, such case with repeat renal pathology converted from a tubulointerstitial lesion to a glomerular lesion has never been reported in literature to date, although predominant tubulointerstitial lesions have been observed both in initial renal biopsy results and repeat biopsy after four years in a previously reported case.[4]

Renal function was initially impaired (serum creatinine, 1.8 mg/dL) in the present case regardless of the good recovery after prednisone treatment. Renal function impairment was the main presentation in the past cases of predominant tubulointerstitial lupus nephritis, and most of which were acute renal failure, while some of the cases received hemodialysis.[3,4,7-16] Therefore, predominant tubulointerstitial lesion in patients with lupus nephritis could cause harm to renal function, the reason for this may be that the interstitial fibrosis would lead to renal dysfunction. Nephrogenic diabetes insipidus is another presentation in the present case, and it was clear that the tubulointerstitial lesion led to arginine vasopressin resistance, followed by the occurrence of nephrogenic diabetes insipidus. However, the prednisone treatment cured this. Nephrogenic diabetes insipidus is really rare and can be seen in patients with Sjögren's syndrome and SLE.[17]

For the treatment of predominant tubulointerstitial lupus nephritis, the present case responded well to moderate doses of prednisone (30 mg/d) without cytotoxic immunosuppressive treatment, suggesting the good response to corticosteroid alone. Since merely few cases of predominant tubulointerstitial lupus nephritis have been reported, there is no established treatment. Furthermore, most of the cases in previous reports were sensitive to corticosteroid alone and did not require the initiation of cytotoxic immunosuppressive therapy.[3,8] The present case was well-controlled merely with prednisone alone for six years, and the patient had no relapse until discontinuing the treatment for one year. Therefore, this rare variant of predominant tubulointerstitial lupus nephritis follows a relatively benign and steroid-responsive course with good prognosis.

4 | CONCLUSION

Predominant tubulointerstitial nephritis presented a patient with SLE and Sjögren's syndrome, although this is rare. However, after the withdrawal of the main treatment of SLE (prednisone treatment), the disease worsened after one year. The repeat renal biopsy results revealed predominant glomerulonephritis and the conversion from tubulointerstitial nephritis to glomerulonephritis.

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CONFLICT OF INTEREST

No conflict of interest to declare.

AUTHORS CONTRIBUTION

NY: collected the data and drafted the manuscript. LL: followed up the patient, involved in the idea of the manuscript, and revised the manuscript.

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